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EXAMINER

STEADMAN, DAVID J

ART UNIT PAPER NUMBER

1656

DATE MAILED: 07/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No. 10/049,429	Applicant(s) SCHLESSINGER ET AL.	
Examiner David J. Steadman	Art Unit 1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 29 April 2005.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-3 is/are pending in the application.
4a) Of the above claim(s) 2 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1 and 3 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on 12 February 2002 is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) All b) Some * c) None of:
- Certified copies of the priority documents have been received.
 - Certified copies of the priority documents have been received in Application No. _____.
 - Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) Notice of References Cited (PTO-892)
- 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) Notice of Informal Patent Application (PTO-152)
- 6) Other: _____

DETAILED ACTION

Status of the Application

[1] The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1656.

[2] Claims 1-3 are pending in the application.

[3] Applicants' amendment to the claims, filed 4/29/2005, is acknowledged. This listing of the claims replaces all prior versions and listings of the claims.

[4] Applicants' amendment to the specification, filed 4/29/2005, is acknowledged.

[5] Receipt of a substitute oath/declaration, filed 1/28/2005, is acknowledged.

[6] Applicant's arguments filed 4/29/2005 have been fully considered and are deemed to be persuasive to overcome some of the rejections and/or objections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

[7] The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Lack of Unity

[8] Claim 2 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 9/24/2004.

[9] Claims 1 and 3 are being examined on the merits.

Oath/Declaration

[10] The objection to the Declaration is withdrawn in view of the substitute oath/declaration.

Sequence Compliance of Drawings

[11] The objection to the drawings as disclosing nucleotide and/or amino acid sequences that do not comply with the requirements of 37 CFR 1.821 through 1.825 is withdrawn in view of applicants' arguments. Applicants argue the specification was amended to bring Figures 4, 15, 17, 20, and 25 in compliance with the sequence listing rules. An amendment to the specification, filed 10/16/2002, identified those nucleotide and/or amino acid sequences disclosed in Figures 4, 15, 17, 20, and 25 by a sequence identifier.

Second Request for Clarification

[12] The specification discloses that the structural coordinates of FGFR1 D2-D3 / FGF1 complex were generated using the D2-D3 domain consisting of amino acids 142-365 of FGFR1 (sentence bridging pp. 61-62). It is unclear from the specification as to the sequence identifier that corresponds to amino acids 142-365 of FGFR1. In order to advance prosecution, the examiner has interpreted amino acids 142-365 of FGFR1 as being identical to SEQ ID NO:1. In other words, the examiner is of the understanding

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that the D2-D3 domain of FGFR1 is SEQ ID NO:1 and that the polypeptide of SEQ ID NO:1 was used in making the FGFR1 D2-D3 / FGF1 complex crystals as disclosed at pp. 88-90 of the specification. The claims have been examined accordingly. If the examiner's understanding is incorrect, applicants are requested to so state and clarify the record and identify which of the sequence identifiers corresponds to the FGFR1 D2-D3 domain.

Specification/Informalities

[13] The objection to the specification for attempting to incorporate subject matter into this application by reference to a hyperlink is withdrawn in view of the amendment to the specification to delete the hyperlink.

[14] The objection to the specification in the use of the trademarks "Centricon 10" and "Superdex 200" (p. 89 of the specification) is withdrawn in view of the amendment to the specification to capitalize all letters of the trademarks. They should be capitalized wherever they appear and be accompanied by the generic terminology.

[15] The objection to the specification as disclosing a description of Figure 4 (p. 27) that does not correspond to the drawing of Figure 4 is maintained for the reasons of record. It appears that applicants have made no attempt to respond to this objection.

[16] The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: --Crystal of Fibroblast Growth Factor Receptor 1 in Complex with Fibroblast Growth Factor--.

Claim Objection(s)

[17] The objections to claims 6-7, 9-10, and 74 are withdrawn in view of the cancellation of these claims.

[18] Claims 1 and 3 are objected to as using inconsistent terminology. Claim 1 recites "FGF-1," while claim 3 recites "FGF1." It is suggested that applicants amend the claims to use consistent terminology.

[19] Claim 3 is objected to as "chararacterized" is misspelled and should be replaced with "characterized." As a point of clarification, it is noted that the term "is chararacterized [sic] by" in claim 3 has been interpreted by the examiner as meaning "has." If applicants intend for the term "is chararacterized [sic] by" to have a meaning other than "has," applicants are requested to so state and clarify the record.

Claim Rejections - 35 USC § 112, Second Paragraph

[20] Claims 1 and 3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection is necessitated by amendment.

[a] Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. It is well-known in the prior art that three repeating vectors, a, b, and c, with angles α , β , and γ , between them, are required to define the unit cell in a crystal lattice. See p. 586 of the "Encyclopedia of Molecular Biology"

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(Creighton, T., John Wiley and Sons, Inc. New York, 1999). This is acknowledged by the specification, which states, "[t]he term 'unit cell' refers to the smallest and simplest volume element of a crystal that is completely representative of the unit of pattern of the crystal... [t]he dimensions of the unit cell are defined by six numbers: dimensions a, b and c and angles α , β , and γ " (p. 10, bottom). As such, each of the six numbers is essential to describe the unit cell of a crystal lattice. In this case, claim 1 omits the value of vector c, which according to the specification, is required to define the unit cell.

[b] Claim 3 is confusing in the recitation of "[a] crystal... characterized by the atomic structure coordinates of Table 2." While Table 2 may disclose the atomic structural coordinates of the FGFR1 D2-D3 / FGF1 complex, the atomic structural coordinates of Table 2 do not characterize the crystal. As noted above, the six numbers of dimensions a, b and c and angles α , β , and γ characterize a crystal. It is suggested that applicants clarify the meaning of the claim.

Claim Rejections - 35 USC § 101

[21] The rejection of claims 5-7 and 9-12 under 35 U.S.C. 101 and the corresponding enablement rejection of claims 5-7 and 9-12 under 35 U.S.C. 112, first paragraph, are withdrawn. The rejections have not been withdrawn in view of applicants' arguments, but have instead been withdrawn upon further consideration by the examiner. It is noted that claims 1 and 3 as amended represent embodiments of original claims 5-7 and 9-12.

Panek et al. (*J Pharmacol Exp Therap* 286:569-577) teaches that a small molecule inhibitor, PD 166866, selectively inhibits FGFR1 and that PD 166866 is a

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"potent" inhibitor of angiogenesis from cultured artery fragments (p. 569, abstract). As such, a skilled artisan would recognize the well-established use of FGFR1 as a target for chemotherapeutic agents and the claimed crystal of FGFR1 complexed with its cognate ligand is useful for generating a three-dimensional structure for identification of agents that inhibit their interaction and thus FGFR1 signaling.

Claim Rejections - 35 USC § 112, First Paragraph

[22] Claim(s) 1 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection that is necessitated by amendment.

MPEP § 2163 states, "when filing an amendment an applicant should show support in the original disclosure for new or amended claims." In this case, the examiner can find no explicit showing of support for the instant amendment to claim 1. At the bottom of p. 4 of the instant response, applicants assert "[t]he examiner has stated...the specification is enabled for 'a crystal of a purified polypeptide of SEQ ID NO:1 co-crystallized with the FGF-1 of SEQ ID NO:17 having a tetragonal space group symmetry P1 and the unit cell dimensions of $a=62.55 \text{ \AA}$, $b=64.14 \text{ [\AA]}$, $\alpha=93.40^\circ$, $\beta=111.17^\circ$, and $\gamma=97.18^\circ$.'" While one may argue this is an implicit showing of support, the examiner made no such remark. The exact remark made by the examiner is, "a crystal of a purified polypeptide of SEQ ID NO:1 co-crystallized with the FGF-1 of SEQ ID NO:17

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having tetragonal space group symmetry P1 and the unit cell dimensions of $a=62.55$, $b=64.06\text{\AA}$, $c=64.14\text{\AA}$, $\alpha=93.40^\circ$, $\beta=111.17^\circ$, and $\gamma=97.18^\circ$." MPEP § 2163 further states, "[i]f the originally filed disclosure does not provide support for each claim limitation, or if an element which applicant describes as essential or critical is not claimed, a new or amended claim must be rejected under 35 U.S.C. 112, para. 1, as lacking adequate written description." In accordance with MPEP § 2163, claim 1 is rejected as lacking support for the claimed limitation. Applicants are invited to show support for the limitation at issue.

[23] The written description rejection of claim(s) 2 under 35 U.S.C. 112, first paragraph, is withdrawn in view of the amendment to claim 2 to recite non-elected subject matter such that the claim has been withdrawn from consideration.

[24] The written description rejection of claim(s) 1 and 3 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons stated below.

RESPONSE TO ARGUMENT: It is noted that applicants' arguments appear to address only the scope of enablement rejection under 35 USC 112, first paragraph, and not the instant written description rejection. To the extent applicants' arguments apply to the instant rejection, these arguments have been addressed below.

Applicants argue claim 1 has been amended to "recite the subject matter that the Examiner has found to be enabled," *i.e.*, "a crystal of a purified polypeptide of SEQ ID NO:1 co-crystallized with the FGF-1 of SEQ ID NO:17 having a tetragonal space group symmetry P1 and the unit cell dimensions of $a=62.55\text{\AA}$, $b=64.14\text{\AA}$, $\alpha=93.40^\circ$, $\beta=111.17^\circ$, and $\gamma=97.18^\circ$." However, as noted above, this is incorrect as the examiner

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stated the specification is enabling for a crystal of a purified polypeptide of SEQ ID NO:1 co-crystallized with the FGF-1 of SEQ ID NO:17 having tetragonal space group symmetry P1 and the unit cell dimensions of $a=62.55 \text{ \AA}$, $b=64.06 \text{ \AA}$, $c=64.14 \text{ \AA}$, $\alpha=93.40^\circ$, $\beta=111.17^\circ$, and $\gamma=97.18^\circ$.

Applicants' argument is not found persuasive. The "Encyclopedia of Molecular Biology" (Creighton, T., John Wiley and Sons, Inc. New York, 1999, p. 586) states that "[i]n the regular packing inside the crystal, three repeating vectors can be recognized: a, b, and c, with angles α , β , and γ , between them. These three vectors define a unit cell in the crystal lattice." This same reference defines "unit cell" (p. 2725) as follows: "[a] crystal is characterized by the regular and periodic arrangement of its parts, which are ions, atoms, or molecules (see Crystallography). In this regular packing, three repeating vectors a, b, and c can be recognized with angles α , β , and γ between them." Also, the specification discloses "[t]he dimensions of the unit cell are defined by six numbers: dimensions a, b and c and angles α , β , and γ " (p. 10, bottom). See also p. 4, ¶ [0031] of US Patent Application Publication 2004/0005686 A1, which states, "[t]he dimensions of a unit cell of a crystal are defined by six numbers, the lengths of three unique edges, a, b, and c, and three unique angles α , β , and γ . The type of unit cell that comprises a crystal is dependent on the value of these variables and the various symmetry elements that are present within the unit cell." In view of the teachings of the specification and the prior art, the values of a, b, and c, with angles α , β , and γ are essential to describe the unit cell of a crystal. However, the crystal of claim 1 fails to recite the value of c. The claim omits a critical or essential element of the claimed crystal, *i.e.*, the value of c. As

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such, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention.

Regarding claim 3, the claim is drawn to a genus of crystals "characterized by the atomic structure coordinates of Table 2." The specification discloses that "the structural coordinates set forth in Tables 1-4 and 6 are not limited to the values defined therein" p. 10, lines 23-24). As such, the genus of FGFR1 D2-D3 / FGF1 protein complex crystals encompass species that are widely variant with respect to their structures. As noted in a previous Office action, while MPEP § 2163 acknowledges that in certain situations "one species adequately supports a genus", it is also acknowledges that "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus." As such, the single disclosed species of FGFR1 D2-D3 / FGF1 protein complex crystals fails to represent all members of the claimed genus. Given the lack of description of a representative number of crystals, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention.

[25] The scope of enablement rejection of claim(s) 3 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons stated below.

Applicants fail to address the rejection of claim 3. Presumably, applicants would argue that the amendment to claim 3 overcomes the instant rejection.

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Claim 3 is drawn to a crystal "characterized by the atomic structure coordinates of Table 2." The specification discloses that "the structural coordinates set forth in Tables 1-4 and 6 are not limited to the values defined therein" p. 10, lines 23-24). As such, the FGFR1 D2-D3 / FGF1 protein complex crystal broadly encompasses a crystal of FGFR1 D2-D3 from any source, including mutants and variants thereof, complexed with FGF1 from any source, including mutants and variants thereof, with a unit cell having any unit cell dimensions. The specification provides only a single working example of the claimed crystal, *i.e.*, a crystal of a purified polypeptide consisting of amino acids 142-365 of FGFR1 (interpreted herein as SEQ ID NO:1) co-crystallized with the FGF-1 of SEQ ID NO:17 having tetragonal space group symmetry P1 and the unit cell dimensions of $a=62.55 \text{ \AA}$, $b=64.06 \text{ \AA}$, $c=64.14 \text{ \AA}$, $\alpha=93.40^\circ$, $\beta=111.17^\circ$, and $\gamma=97.18^\circ$ (see pp. 61-62 of the specification). Other than this single working example, the specification fails to disclose additional FGFR1 D2-D3 / FGF1 protein complex crystal forms. In view of the lack of guidance and working examples, it is highly unpredictable as to whether other X-ray diffraction-quality crystals can be generated that will yield additional structural coordinates for a FGFR1 D2-D3 / FGF1 protein complex as evidenced by Branden et al. (cited in a previous Office action). Further, it is not routine in the art to generate additional crystal forms of a polypeptide complex to provide for additional structural coordinates. In view of this analysis of the relevant Factors of *In re Wands*, the specification fails to enable the full scope of claimed crystals without undue experimentation.

Claim Rejections - 35 USC § 102

[26] The rejection of claims 1-2, 8, and 69 under 35 U.S.C. 102(b) as being anticipated by Wiesmann et al. (*Cell* 91:695-704) is withdrawn in view of the amendment to claims 1-2 and cancellation of claims 8 and 69. Wiesmann et al. does not teach or suggest the crystal of claim 1.

Claim Rejections - 35 USC § 103

[27] The rejection of claim(s) 17 under 35 U.S.C. 103(a) as being unpatentable over Wiesmann et al. in view of the state of the art at the time of the invention is withdrawn in view of the cancellation of claim 17.

Conclusion

[28] Status of the claims:

- Claims 1-3 are pending.
- Claim 2 is withdrawn from further consideration.
- Claims 1 and 3 are rejected.
- No claim is in condition for allowance.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the


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shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Steadman whose telephone number is 571-272-0942. The examiner can normally be reached on Monday to Friday, 7:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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Art Unit 1656